

In the Drawing:

Please amend original Figs. 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, and 13 individually as shown in red ink within enclosed Substitute Figs. 2-13 respectively.

In the Claims:

~~Cancel~~ original claim 18, without prejudice.

Amend original claims 1-3 and 12-14 respectively, as follows.

GB 08

1 (Once Amended). A prepared DNA segment for placement in a suitable expression vector and transfection of endothelial cells in-situ such that overexpression of extracellular matrix heparan sulphate proteoglycans subsequently occurs in-situ, said prepared DNA segment comprising:

at least one first DNA sequence coding for the extracellular domain of a discrete proteoglycan entity that is expressed by a transfected endothelial cell in-situ after being transfected with said first DNA sequence, said extracellular domain first DNA sequence specifying the extracellular N-terminal portion of an expressed proteoglycan entity which is then located at and extends from the endothelial cell surface and is capable of binding heparan sulfates to form an extracellular matrix in-situ;

at least one second DNA sequence coding for the transmembrane domain of a discrete proteoglycan entity that is expressed by a transfected endothelial cell in-situ after being transfected with said second DNA sequence, said transmembrane domain second DNA sequence specifying the medial portion of an expressed proteoglycan entity which is

then located at and extends through the endothelial cell membrane and is joined with said extracellular N-terminal portion of said expressed proteoglycan entity; and

at least one third DNA sequence coding for the cytoplasmic domain of the syndecan-4 molecule in said discrete proteoglycan entity that is expressed by a transfected endothelial cell in-situ after being transfected with said third DNA sequence, said syndecan-4 cytoplasmic domain third DNA sequence specifying the cytoplasmic portion of an expressed proteoglycan entity which is then present within the cytoplasm of a transfected endothelial cell and is joined to said transmembrane portion and said extracellular N-terminal portion of said expressed proteoglycan entity.

2 (Once Amended). A constructed expression vector for transfection of endothelial cells in-situ such that overexpression of extracellular matrix heparan sulfate proteoglycan subsequently occurs in-situ, said constructed expression vector comprising:

a prepared DNA segment comprised of

(i) at least one first DNA sequence coding for the extracellular domain of a discrete proteoglycan entity that is expressed by a transfected endothelial cell in-situ after being transfected with said first DNA sequence, said extracellular domain first DNA sequence specifying the extracellular N-terminal portion of an expressed proteoglycan entity which is then located at and extends from the endothelial cell surface and is capable of binding heparan sulfates to form an extracellular matrix in-situ,

(ii) at least one second DNA sequence coding for the transmembrane domain of a discrete proteoglycan entity that is expressed by a transfected endothelial cell in-situ after being transfected with said second DNA sequence, said transmembrane

domain second DNA sequence specifying the medial portion of an expressed proteoglycan entity which is then located at and extends through the endothelial cell membrane and is joined with said extracellular N-terminal portion of said proteoglycan entity, and

(iii) at least one third DNA sequence coding for the cytoplasmic domain of the syndecan-4 molecule in said discrete proteoglycan entity that is expressed by a transfected endothelial cell in-situ after being transfected with said third DNA sequence, said syndecan-4 cytoplasmic domain third DNA sequence specifying the cytoplasmic portion of an expressed proteoglycan entity and is then present within the cytoplasm of a transfected endothelial cell and is joined to said transmembrane portion and said extracellular N-terminal portion of said expressed proteoglycan entity; and
an expression vector carrying said prepared DNA segment and suitable for transfection of endothelial cells in-situ.

3 (Once Amended). An in-situ transfected endothelial cell which overexpresses extracellular matrix heparan sulfate proteoglycans and positions [on] the proteoglycans at the cell surface, said in-situ transfected endothelial cell comprising:

a viable endothelial cell previously transfected in-situ with a constructed expression vector such that said transfected endothelial cell overexpresses discrete extracellular matrix heparan sulfate proteoglycan entities coded for by said vector, said overexpressed proteoglycan entities being comprised of

(i) an extracellular N-terminal portion which is located at and extends from the transfected endothelial cell surface and which binds heparan sulfates to form an extracellular matrix in-situ, said extracellular N-terminal portion being the expressed

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product of at least one first DNA sequence in the [prepared] constructed expression vector coding for the extracellular domain of said proteoglycan entity expressed by the transfected endothelial cell in-situ,

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(ii) a transmembrane medial portion which is located at and extends through the endothelial cell membrane and is joined with said extracellular N-terminal portion of said proteoglycan entity, said transmembrane medial portion being the expressed product of at least one second DNA sequence in the prepared expression vector coding for the transmembrane domain of said proteoglycan entity expressed by the transfected endothelial cell in-situ, and

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(iii) a syndecan-4 cytoplasmic portion present within the cytoplasm of the transfected endothelial cell which is joined to said transmembrane portion and said extracellular N-terminal portion of said proteoglycan entity, said syndecan-4 cytoplasmic portion being the expressed product of at least one third DNA sequence in the [prepared] constructed expression vector coding for the cytoplasmic domain of the syndecan-4 molecule of said proteoglycan entity expressed by the transfected endothelial cell in-situ.

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12 (Once Amended). A method for making a prepared DNA segment intended for placement in a suitable expression vector and transfection of endothelial cells in-situ such that overexpression of extracellular matrix heparan sulfate proteoglycan entities subsequently occurs in-situ, said method comprising the steps of:

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obtaining at least one first DNA sequence coding for the extracellular domain of a discrete proteoglycan entity that is expressed by a transfected endothelial cell in-situ after being transfected with said first DNA sequence, said extracellular domain first DNA

sequence specifying the extracellular N-terminal portion of an expressed proteoglycan entity which is then located at and extends from the transfected endothelial cell surface and is capable of binding heparan sulfates to form an extracellular matrix in-situ;

acquiring at least one second DNA sequence coding for the transmembrane domain of a discrete proteoglycan entity that is expressed by a transfected endothelial cell in-situ after being transfected with said second DNA sequence, said transmembrane domain second DNA sequence specifying the medial portion of an expressed proteoglycan entity which is then located at and extends through the transfected endothelial cell membrane and is joined with said extracellular N-terminal portion of said expressed proteoglycan entity;

procuring at least one third DNA sequence coding for the cytoplasmic domain of the syndecan-4 molecule in said discrete proteoglycan entity that is expressed by a transfected endothelial cell in-situ after being transfected with said third DNA sequence, said syndecan-4 cytoplasmic domain third DNA sequence specifying the cytoplasmic portion of an expressed proteoglycan entity which is then present within the cytoplasm of [a] said transfected endothelial cell and is joined to said transmembrane portion and said extracellular N-terminal portion of said expressed proteoglycan entity; and

joining together said extracellular domain first DNA sequence, said transmembrane domain second DNA sequence, and said syndecan-4 cytoplasmic domain third DNA sequence as a discrete prepared DNA segment.

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13 (Once Amended). A method for making a constructed expression vector intended for transfection of endothelial cells in-situ such that overexpression of extracellular matrix

heparan sulfate proteoglycans subsequently occurs in-situ, said method comprising the steps of:

obtaining a prepared DNA segment comprised of

(i) at least one first DNA sequence coding for the extracellular domain of a discrete proteoglycan entity that is expressed by a transfected endothelial cell in-situ after being transfected with said first DNA sequence, said extracellular domain first DNA sequence specifying the extracellular N-terminal portion of an expressed proteoglycan entity which is then located at and extends from the transfected endothelial cell surface and is capable of binding heparan sulfates to form an extracellular matrix in-situ,

(ii) at least one second DNA sequence coding for the transmembrane domain of a discrete proteoglycan entity that is expressed by a transfected endothelial cell in-situ after being transfected with said second DNA sequence, said transmembrane domain second DNA sequence specifying the medial portion of an expressed proteoglycan entity which is then located at and extends through the transfected endothelial cell membrane and is joined with said extracellular N-terminal portion of said expressed proteoglycan entity, and

(iii) at least one third DNA sequence coding for the cytoplasmic domain of the syndecan-4 molecule in a discrete proteoglycan entity that is expressed by a transfected endothelial cell in-situ after being transfected with said third DNA sequence, said syndecan-4 cytoplasmic domain third DNA sequence specifying the cytoplasmic portion of an expressed proteoglycan entity which is then present within the cytoplasm of [a] said transfected endothelial cell and is joined to said transmembrane portion and said extracellular N-terminal portion of said expressed proteoglycan entity; and

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positioning said prepared DNA segment into an expression vector suitable for transfection of endothelial cells *in-situ*.

14 (Once Amended). A method for stimulating angiogenesis *in-situ* within living tissues comprising vascular endothelial cells, said method comprising the steps of:

transfected vascular endothelial cells *in-situ* with a constructed expression vector such that the resulting transfected vascular endothelial cells overexpress discrete extracellular matrix heparan sulphate proteoglycan entities coded for by said constructed expression vector, said overexpressed proteoglycan entities being comprised of

(i) an extracellular N-terminal portion which is located at and extends from a transfected vascular endothelial cell surface and binds heparan sulphates to form an extracellular matrix *in-situ*, said extracellular N-terminal portion being the expressed product of at least one first DNA sequence in the constructed expression vector coding for the extracellular domain in a proteoglycan entity expressed by a transfected vascular endothelial cell *in-situ* after being transfected with said first DNA sequence,

(ii) a transmembrane medial portion which is located at and extends through a transfected vascular endothelial cell membrane and is joined with said extracellular N-terminal portion of said expressed proteoglycan entity, said transmembrane medial portion being the expressed product of at least one second DNA sequence in the constructed expression vector coding for the transmembrane domain of said proteoglycan entity expressed by a transfected vascular endothelial cell *in-situ* after being transfected with said second DNA sequence, and